REMARKS

Reconsideration and allowance of the above-referenced application are respectfully requested.

The specification has been amended in order to correct various inadvertent errors noted by the Examiner.

Claims 16, 17 and 22 have been cancelled, and claims 1, 2, 3, 8, 9, 10 and 14 have been amended.

Rejection of Claims 3 and 10 Under 35 U.S.C. 112, First Paragraph

The Examiner has rejected claims 3-10 under Section 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The Examiner's Position

The Examiner contends that all of the monoclonal antibodies recited in the claims are all required in order to practice the claimed invention since each is specifically recited. Thus, the Examiner notes that Applicant must comply with the deposit rules or demonstrate that each antibody is well-known and readily available to the public.

The Applicants' Position

The Applicants respectfully request that the Examiner take notice of the amendments to claims 3 and 10 presented above. Further, it should be noted that the 8 cell lines remaining in claims 3 and 8 are readily available to the public. In particular, it is submitted that hybridoma cell lines 107-35-54 (referred to as H35C54), 110-81-17, 13-975-157 and 14-1350-210 are disclosed in U.S. Patent No. 5,753,430, a copy of which is attached. Further, hybridoma cell lines HC11-14, HC-11-10, HC11-3 and HC11-7 are disclosed in a published PCT application(International Publication No. WO 00/07023) (as well as in PCT application International Publication No. WO 99/06836) and were deposited with the National Research Institute of Microorganisms on July 4, 1987 as FERM BP-6006, FERM BP-6004, FERM BP-6002 and FERM BP-6003. (See attached translation of PCT application WO 00/07023.) Thus, the monoclonal antibodies recited in amended claims 3 and 10 are well-known and readily available to the public. Consequently, it is respectfully requested that the rejection be withdrawn.

Rejection of Claim 22 Under 35 U.S.C. 102(a)

The Examiner has rejected claim 22 under Section 102(a) as being anticipated by Dawson et al.

It is submitted that the rejection is now moot in view of the cancellation of claim 22; thus, the rejection should be withdrawn accordingly.

Rejection of Claims 16, 17 and 22 Under 35 U.S.C. 102(e)

The Examiner has rejected claims 16, 17 and 22 under Section 102(e) as being anticipated to U.S. Patent No. 6,383,740 (Collins).

Applicants submit that the rejection is now moot in view of the cancellation of claims 16, 17 and 22; thus, the rejection should be withdrawn accordingly.

Rejection of Claim 16 Under 35 U.S.C. 102(b)

The Examiner has rejected claim 16 under Section 102(b) as being anticipated by Masalova et al.

In view of the cancellation of claim 16, Applicants submit that the rejection is now moot and should be withdrawn accordingly.

Rejection of Claims 1, 2, 16 and 22 Under 35 U.S.C. 102(b)

The Examiner has rejected claims 1, 2, 16 and 22 (now claims 1 and 2) under Section 102(b) as being anticipated by Jolivet-Reynaud et al.

The Examiner's Position

The Examiner contends that Jolivet-Reynaud et al. disclose the detection of both HCV core antigen (using a sandwich immunoassay with two murine anti-HCV antibodies) and HCV core antibodies (using synthetic HCV core peptides coated on a solid phase).

The Applicants' Position

The Applicants respectfully traverse the rejection of claims 1 and 2 under Section 102(b) as being anticipated by Jolivet-Reynaud et al.

It is submitted that Jolivet-Reynaud et al. disclose the use of two separate assays for the detection of HCV antigen and HCV antibody, respectively. In one assay, HCV core is detected by the use of monoclonal antibodies. In another assay, HCV antibodies are detected by use of a peptide-coated solid phase. However, the reference does not disclose or suggest the use of mixed or blended reagents (i.e., an antigen and an antibody) in order to simultaneously detect HCV antibody and HCV antigen in a test sample, as in the claimed invention. Thus, the claimed invention is certainly not anticipated under Section 102(b) by Jolivet-Reynaud et al., as the reference does not teach the elements of the claimed invention. The

rejection has been overcome and should be withdrawn accordingly.

Rejection of Claims 1-17 Under 35 U.S.C. 103(a)

The Examiner has rejected claims 1-17 under Section 103(a) over Dawson et al. in view of Masalova et al.

The Examiner's Position

The Examiner contends that Dawson et al. disclose co-detection of HCV core antigen and HCV antibodies in a chemiluminescent assay but do not specifically disclose a solid-phase immunoassay format, the use of HCV core monoclonal antibodies, or kits. Additionally, the Examiner asserts that Masalova et al. disclose the use of a solid-phase immunoassay format, sandwich immunoassays and HCV core monoclonal antibodies. Thus, the Examiner alleges that it would have been obvious to one of ordinary skill in the art, at the time the invention was made, to use the conventional solid-phase format, sandwich assays, and HCV core monoclonal antibodies of Masalova et al. in the co-detection assays of Dawson et al. because Masalova et al. teach the successful use of such assay formats and monoclonal antibodies for the detection of HCV core antigen early after HCV infections. Further, the Examiner notes that while neither Dawson et al. nor Masalova et al.

specifically disclose kits, it would have been obvious to one of ordinary skill in the art at the time the invention was made to package components to be used together in the form of a kit for reasons of convenience and economy.

The Applicants' Position

The Applicants respectfully traverse the rejection of claims 1-17 (now 1-15) under Section 103(a) as being obvious over Dawson et al. in view of Masalova et al.

It is submitted that Dawson et al. disclose the "co-detection" of HCV antibodies and HCV antigens; however, Dawson et al. certainly do not disclose or suggest the use of a mixture of reagents (e.g., an HCV antigen and an HCV antibody) in a simultaneous detection method or single assay system designed to detect both HCV antigen and HCV antibody in a single test sample, as in the claimed invention. Rather, Dawson et al. disclose the detection of both HCV antigens and HCV antibodies, by use of separate assays, after seroconversion has occurred.

Further, it is submitted that the Masalova et al. reference does not remedy the deficiencies present in Dawson et al. Masalova et al. disclose the detection of HCV core protein using a monoclonal antibody sandwich enzyme immunoassay. Masalova et al., however, do not disclose or suggest an immunoassay involving detection of

both HCV antigen and HCV antibody by use of a mixture of reagents in a single assay system.

In view of the above, it is submitted that the Section 103(a) rejection of claim 1-15 over Dawson et al. in view of Masalova et al. has been overcome. One of ordinary skill in the art certainly would not have been motivated to have created the claimed invention based upon the teachings or suggestions of Dawson et al., either alone or in combination with Masalova et al. The claimed invention is not rendered obvious, and the rejection should therefore be withdrawn.

Rejection of Claims 3-15 and 17 Under 35 U.S.C. 103(a)

The Examiner has rejected claims 3-15 and 17 (now 3-15) under Section 103(a) as being obvious over U.S. Patent No. 5,627,026 (O'Connor et al.) in view of Jolivet-Reynaud et al.

The Examiner's Position

The Examiner contends that O'Connor et al. teach the simultaneous detection of antigen and antibody, in a sample, and the packaging of the components in the form of a kit. Additionally, the Examiner acknowledges that O'Connor et al. do not specifically teach hepatitis C antigen and hepatitis C antibody.

Further, the Examiner asserts that Jolivet-Reynaud et al. teach the detection of both HCV core antigen using a sandwich immunoassay with two murine anti-HCV antibodies and HCV core antibodies using synthetic HCV core peptides coated on a solid phase. The Examiner acknowledges that neither O'Connor et al. nor Jolivet-Reynaud et al. teach use of a conjugate comprising an antibody attached to a chemiluminescent compound.

In summary, the Examiner contends that it would have been obvious to one of ordinary skill in the art at the time the invention was made to have used the combination hepatitis C antigen and hepatitis C antibody assay format of Jolivet-Reynaud in the simultaneous hepatitis antigen-antibody detection of O'Connor et al. since Jolivet-Reynaud et al. teach an assay for both hepatitis C antigen and hepatitis C antibody, and because O'Connor et al. teach the desirability of simultaneous hepatitis antigen-antibody detection for screening of blood. Further, the Examiner states that use of a chemiluminescent label in place of the avidin-biotin system or the label of O'Connor or Jolivet-Reynaud would have been obvious since all are conventional labeling systems.

The Applicants' Position

The Applicants respectfully traverse the rejection of claims 1-15 under Section 103(a) as being obvious over O'Connor et al. in view of Jolivet-Reynaud et al.

Applicants submit that O'Connor et al. disclose a method for simultaneously detecting the presence of an antibody and an antigen in a biological sample. More specifically, O'Connor et al. disclose the use of separate spots on the filter matrix for: 1) antigen-coated microparticles and 2) antibody-coated microparticles. In contrast, in the claimed invention, a mixture or blend of antigen- and antibody-coated microparticles are utilized.

Additionally, O'Connor et al. disclose the use of a labeled antigen, rather than a labeled antibody, to detect the antibody in a sample (see col. 4, lines 2-4). In contrast, in the claimed invention, a labeled antibody is utilized to detect the antibody in the test sample.

Also, the method of O'Connor et al. produces two independent and distinguishable signals as a result of the application of two separate spots on the filter (i.e., one for the antigen and one for the antibody). In contrast, in the claimed invention, only one signal is produced since the antigen and antibody solid phases as well as conjugates are mixed together.

Further, it should be noted that the Jolivet-Reynaud et al. document does not remedy the deficiencies present in O'Connor et al. More specifically, as noted above, Jolivet-Reynaud et al. disclose the use of two separate assays for the detection of HCV antigen and HCV antibody, respectively. In one assay, HCV core is detected by the use of monoclonal antibodies. In another assay, HCV antibodies are detected by use of a peptide-coated solid phase. However, the reference does not disclose or suggest the use of mixed or blended reagents (i.e., an antigen and an antibody) in order to simultaneously detect HCV antibody and HCV antigen in a test sample, as in the claimed invention. Thus, Jolivet-Reynaud et al. would not have motivated one of ordinary skill in the art, at the time the invention was made, to have utilized a mixture of reagents in the method of O'Connor et al.

In view of the above, it is submitted that the Section 103(a) rejection of claims 3-15 and 17 (now 3-15) as being obvious over O'Connor et al. in view of Jolivet-Reynaud et al. has been overcome. One of ordinary skill in the art certainly would not have been motivated to have created the claimed method based upon the disclosures or suggestions of the cited references, either alone or in combination. The

claimed invention is not rendered obvious, and the rejection should be withdrawn accordingly.

In conclusion, it is believed that the subject application is in condition of allowance and Notice to that effect is respectfully requested.

Should any questions arise concerning the above, the Examiner is respectfully requested to contact the undersigned at the telephone number listed below.

Respectfully submitted,

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MARKED UP VERSION OF SPECIFICATION AND CLAIMS SHOWING CHANGES MADE

IN THE SPECIFICATION:

Please amend the specification as follows:

Please amend page 14, line 25 - page 15, line 18 as follows:

The antibodies which are coated on the solid phase as well as the "second antibody" may be, as noted above, monoclonal antibodies or polyclonal antibodies. For example, if one chooses to utilize monoclonal antibodies, they may be selected from 13-959-270, 14-1269-281, 14-1287-252, 14-153-234, 14-153-462, 14-1705-225, 14-1708-269, 14-1708-403, 14-178-125, 14-188-104, 14-283-112, 14-635-225, 14-726-217, 14-886-216, 14-947-104 and 14-945-218[, all of which have been deposited with the American Type Culture Collection (ATCC), 10801 University Boulevard, Manassas, VA 20110 on _____ and accorded the following accession numbers respectively, _____]. The following anti-core monoclonal antibodies may also be utilized for purposes of the present invention: 107-35-54, 110-81-17, 13-975-157, 14-1350-210 (see U.S. Patent No. 5,753,430) and Tonen HCV core monoclonals C11-3, 7, 10, 14 and 15 (see PCT Application WO 099/06836), all of which are available from the American Type Culture Collection. (For a discussion of the manner in which monoclonal antibodies may be created, see Kohler and Milstein, Nature (1975) 256:494, and reviewed in Monoclonal Hybridoma Antibodies: Techniques and Applications, ed. Hurrell (CRC Press, Inc., 1982); see also J.W. Goding in *Monoclonal Antibodies: Principles and*

Practice (Academic Press, N.Y., 1983; see also U.S. Patent No. 5,753,430).

Please amend Table I on page 18, line 15 - line 36, as follows:

TABLE I
HCV-Core Derived Peptides

Peptide	**Sequence**		**Core Reg. Repr.**
A	MSTNPKPQKKNKRNTNRR	(SEQ ID NO:46)	1-18
B	NKRNTNRRPQDVKFPGGG	(SEQ ID NO:47)	11-28
C	DVKFPGGGQIVGGVYLLP	(SEQ ID NO:48)	21-38
D	VGGVYLLPRRGPRLGVRA	(SEQ ID NO:49)	31-48
E	GPRLGVRATRKTSERSQP	(SEQ ID NO:50)	41-58
F	KTSERSQPRGRRQPIPKA	(SEQ ID NO:51)	51-68
G	RRQPIPKARRPEGRTWAQ	(SEQ ID NO:52)	61-78
H	PEGRTWAQPGYPWPLYGN	(SEQ ID NO:53)	71-88
I	QYPWPLYGNEGCGWAGWLL	(SEQ ID NO:54)	81-98
J	CGWAGWLLSPRGSRPSW	(SEQ ID NO:55)	91-107
1	WLLSPRGSRPSWGPTDPRRRSRNLG	(SEQ ID NO:56)	96-120
2	SWGPTDPRRRSRNLGKVIDTLTCGF	(SEQ ID NO:57)	106-130
3	SRNLGKVIDTLTCGFADLMGYIPLV	(SEQ ID NO:58)	116-140
4	LTCGFADLMGYIPLVGAPLGGAARA	(SEQ ID NO:59)	126-150
5	YIPLVGAPLGGAARALAHGVRVLED	(SEQ ID NO:60)	136-160
6	GAARALAHGVRVLEDGVNYATGNLP	(SEQ ID NO:61)	146-170
7	LEDGVNYATGNLPGCSFSIFLLA	(SEQ ID NO:62)	158-180
8	LPGCSFSIFLLALLSCLTVPASA	(SEQ ID NO:63)	169-191

Please amend page 38, line 14, as follows:

A1. Preparation of r-antigen coated [microaprticles] microparticles

IN THE CLAIMS:

Please amend claims 1, 2, 3, 8, 9, 10 and 14 as follows:

1. (amended) A method of [simutaneously] simultaneously detecting at least one Hepatitis C Virus (HCV) antigen and at least one HCV antibody in a test sample comprising [the steps of:

a)] contacting said test sample with a mixture of:

1) at least one HCV [viral] antigen or portion thereof coated on a solid phase, for a time and under conditions sufficient for the formation of antibody/antigen complexes, presence of said antibody/antigen complexes indicating presence of said at least one HCV antibody in said test sample; and

2) at least one antibody to HCV or portion thereof coated on said solid phase, for a time and under conditions sufficient for the formation of antigen/antibody complexes[;

b) detecting said antibody/antigen complexes,] presence of said antigen/antibody complexes indicating presence of said at least one HCV antigen in said test sample[; and

c) detecting said antigen/antibody complexes, presence of said complexes indicating presence of HCV antibody in said test sample].

2. (amended) The method of claim 1 wherein said at least one HCV antigen coated on the solid phase is selected from the group consisting of core antigen, NS3, NS4[,] and NS5[, and portions thereof].

3. (amended) The method of claim 2 wherein said at least one antibody coated on said solid phase is a monoclonal antibody selected from the group consisting of [13-959-270, 14-1269-281, 14-1287-252, 14-153-234, 14-153-462, 14-1705-225, 14-1708-269, 14-1708-403, 14-178-125, 14-188-104, 14-283-112, 14-635-225, 14-726-217, 14-886-216, 14-947-104, 14-945-218,] 107-35-54, 110-81-17,

13-975-157, 14-1350-210, C11-3, C11-7, C11-10[,] and C11-14 [and C11-15].

8. (amended) A method for simultaneously detecting the presence of at least one HCV antigen and at least one HCV antibody in a test sample comprising the steps of:

a) contacting said test sample with: 1) at least one HCV [viral] antigen or portion thereof coated on a solid phase, for a time and under conditions sufficient for the formation of antibody/antigen complexes and 2) at least one HCV antibody or portion thereof coated on said solid phase, for a time and under conditions sufficient for the formation of antigen/antibody complexes;

b) adding a conjugate to the resulting antibody/antigen complexes of (a)(1) for a time and under conditions sufficient to allow said conjugate to bind to the bound antibody in (a)(1), wherein said conjugate comprises a second antibody attached to a chemiluminescent compound capable of generating a detectable signal; and simultaneously adding a second conjugate to the resulting antigen/antibody complexes of (a)(2) for a time and under conditions sufficient to allow said conjugate to bind to the bound antigen in (a)(2), wherein said conjugate comprises a third antibody attached to said chemiluminescent compound capable of generating a detectable signal; and

c) detecting said generated signal, presence of said signal indicating presence of [at least one antigen in said test sample selected from the group consisting of] said at least one HCV antigen, [and] at least one HCV antibody, or both, in said test sample.

9. (amended) The method of claim 8 wherein said at least one HCV antigen coated on the solid phase is selected from the group consisting of core antigen, NS3, NS4[,] and NS5[, and portions thereof].

10. (amended) The method of claim 9 wherein said at least one antibody coated on said solid phase is a monoclonal antibody selected from the group consisting of [13-959-270, 14-1269-281, 14-1287-25, 14-153-234, 14-153-462, 14-1705-225, 14-1708-269, 14-1708-403, 14-178-125, 14-188-104, 14-283-112, 14-635-225, 14-726-217, 14-886-216, 14-947-104, 14-945-218, 13-975-157 and 14-1350-210,] 107-35-54, 110-81-17, C11-3, C11-7, C11-10[,] and C11-14 [and] C11-15.

13. (amended) The kit of claim 12 or claim 13 further comprising at least one conjugate comprising a signal-generating compound attached to an antibody.